

**REMARKS****Status of the Claims**

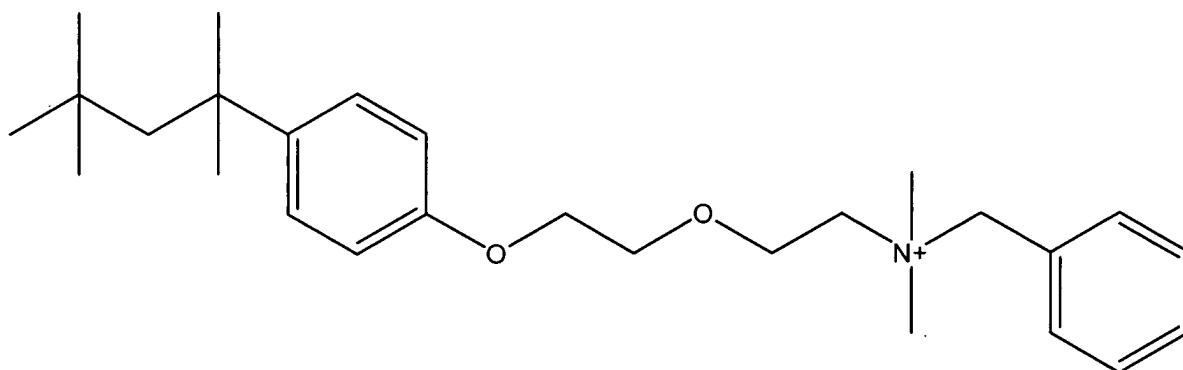
Claims 47-56 were previously pending. Claims 47-50 have been allowed. Claim 89 has been added, support for which can be found, for example, in Example 1. Accordingly claims 51-56 and 89 are at issue.

**Rejections Under 35 U.S.C. §112, first paragraph**

Claims 51 -56 stand rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. The Examiner contends that while the specification is enabled for the benzethonium salt in the examples (i.e., benzethonium chloride), it is not enabled for formulations comprising any benzethonium salt. The Examiner further states that "[t]he predictability [sic: unpredictability] in this art is high since a small change . . . could result in a drastic change in activity . . ."

Applicants respectfully traverse this rejection and request reconsideration.

The term "benzethonium" denotes a specific quaternary ammonium ion, which is set forth below:



Consequently, the term "benzethonium salt" (which is recited in claim 51 as "a benzethonium salt" merely to provide correct antecedent basis) has only one variable component, i.e., the anion.

It is well-known in the art that the microbiocidal activity of quaternary ammonium compounds lies in the quaternary ammonium cation, not the anion. Ullman's Encyclopedia of Industrial Chemistry ("Ullman"), 5<sup>th</sup> Ed. (1990) (Exhibit A) characterizes the entire class of quaternary ammonium compounds as microbiocides:

Quaternary ammonium compounds are most effective against gram-positive bacteria at concentrations as low as 1:200 000. ...

(Exhibit A, p. 566). Ullman does not disclose or suggest that only the chloride salts of quaternary ammonium compounds are microbiocidal. In fact, several non-chloride quaternary ammonium compounds have been shown to be anti-microbial. For example, the propionate salt of didecylmethylpoly(oxyethyl)ammonium is sold as a disinfectant (Exhibit B). See also, col. 3, lines 61-62, and col. 5, lines 45-61, of U.S. Patent No. 5,753,600 (disclosing that the anion of an antibacterial benzalkonium salt can be, for example, an amino acid, fatty acid, or an anionic residue of phosphate, phosphonate, sulfonate, or sulfate having an alkyl or alkenyl group of branched or straight chain 1-30 carbon atoms).

Furthermore, several issued U.S. patents refer to benzethonium salts generally as antimicrobial agents. See, for example, claim 3 and col. 3, lines 12-17, of U.S. Patent No. 6,790,460; claims 8, 27, 36, and 45 of U.S. Patent No. 6,057,015.

Additionally, a chloride anion alone is biocidally inactive up to rather high concentration (otherwise there would be no life in the ocean). Therefore, the activity of benzethonium chloride clearly resides in the benzethonium cation, not the chloride anion.

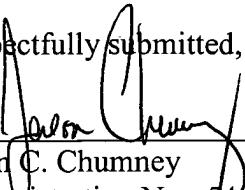
For the foregoing reasons, the claims are enabled for benzethonium salts generally. Accordingly, applicants respectfully request withdrawal of this rejection.

Applicants do not understand the last sentence in the first paragraph of page 3 of the Office Action, which states that "[t]he group of benzethonium salts created should be structurally similar to benzethonium salts." Applicants respectfully request clarification of this statement.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Dated: December 22, 2005

Respectfully submitted,

By   
Jason C. Chumney

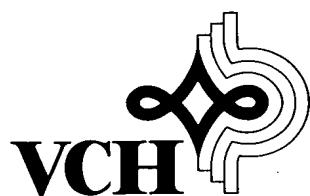
Registration No.: 54,781  
DARBY & DARBY P.C.  
P.O. Box 5257  
New York, New York 10150-5257  
(212) 527-7700  
(212) 527-7701 (Fax)  
Attorneys/Agents For Applicant

# Ullmann's Encyclopedia of Industrial Chemistry

Fifth, Completely Revised Edition

Volume A 16:  
Magnetic Materials to Mutagenic Agents

Editors: Barbara Elvers, Stephen Hawkins, Gail Schulz



*Numerical data, descriptions of methods or equipment, and other information presented in this book have been carefully checked for accuracy. Nevertheless, authors and publishers do not assume any liability for misprints, faulty statements, or other kinds of errors. Persons intending to handle chemicals or to work according to information derived from this book are advised to consult the original sources as well as relevant regulations in order to avoid possible hazards.*

Production Director: Maximilian Montkowski

Production Manager: Myriam Nothacker

Library of Congress Card No. 84-25-829

Deutsche Bibliothek, Cataloguing-in-Publication Data:

**Ullmann's encyclopedia of industrial chemistry** / ed.: Barbara Elvers ... [Ed. advisory board Hans-Jürgen Arpe ...]. — Weinheim ; Basel (Switzerland) ; Cambridge ; New York, NY : VCH.

Teilw. executive ed.: Wolfgang Gerhartz

Bis 4. Aufl. u. d. T.: Ullmanns Encyklopädie der technischen Chemie

NE: Gerhartz, Wolfgang [Hrsg.]; Elvers, Barbara [Hrsg.]; Encyclopedia of industrial chemistry

Vol. A. Alphabetically arranged articles.

16. Magnetic materials to mutagenic agents. — 5., completely rev. ed. — 1990

ISBN 3-527-20116-5 (Weinheim ...)

ISBN 0-89573-166-5 (New York)

#### **British Library Cataloguing in Publication Data**

Ullmann's encyclopedia of industrial chemistry.

Vol. A 15, Isotopes, Natural to Magnesium Compounds

1. Industrial chemistry

I. Elvers, Barbara II. Rounsville, James F. III. Schulz, Gail

661

ISBN 3-527-201116-5

© VCH Verlagsgesellschaft mbH, D-6940 Weinheim (Federal Republic of Germany), 1990.

Printed on acid-free paper

#### **Distribution**

VCH Verlagsgesellschaft, P.O. Box 101161. D-6940 Weinheim (Federal Republic of Germany)

Switzerland: VCH Verlags-AG, P.O. Box, CH-4020 Basel (Switzerland)

Great Britain and Ireland: VCH Publishers (UK) Ltd., 8 Wellington Court, Wellington Street, Cambridge CB1 1HZ (Great Britain)

USA and Canada: VCH Publishers, Suite 909, 220 East 23rd Street, New York NY 10010-4606 (USA)

All rights reserved (including those of translation into other languages). No part of this book may be reproduced in any form — by photoprint, microfilm, or any other means — transmitted or translated into a machine language without written permission from the publishers.

Authorization to photocopy items for internal or personal use, or the internal or personal use of specific clients, is granted for libraries and other users registered with the Copyright Clearance Center (CCC) Transactional Reporting Service, provided that the base fee of \$ 1.00 per copy, plus \$ 0.25 per page is paid directly to CCC, 27 Congress Street, Salem, MA 01970. 0740-9451/85 \$ 1.00 + 0.25. Registered names, trademarks, etc. used in this book and not specifically marked as such are not to be considered unprotected.

Cover design: Wolfgang Schmidt

Composition, printing, and bookbinding: Graphischer Betrieb Konrad Tritsch, D-8700 Würzburg

Printed in the Federal Republic of Germany

# Microbiocides

KEN R. PAYNE, Chesterfield, United Kingdom (Chap. 1)

EDWARD HILL, ECHA Microbiology Limited, Cardiff, United Kingdom (Chap. 2)

<b>1.</b>	<b>Chemical Biocides . . . . .</b>	564
<b>1.1.</b>	<b>Phenolics . . . . .</b>	564
<b>1.2.</b>	<b>Chlorine and Chlorine-Releasing Compounds . . . . .</b>	565
<b>1.3.</b>	<b>Iodine and Iodophores . . . . .</b>	566
<b>1.4.</b>	<b>Quaternary Ammonium Compounds . . . . .</b>	566
<b>1.5.</b>	<b>Biguanides . . . . .</b>	566
<b>1.6.</b>	<b>Peroxygens . . . . .</b>	567
<b>1.7.</b>	<b>Alcohols . . . . .</b>	567
<b>1.8.</b>	<b>Aldehydes . . . . .</b>	567
<b>1.9.</b>	<b>Hydroxybenzoate Esters . . . . .</b>	568
<b>1.10.</b>	<b>Heavy Metals . . . . .</b>	568
<b>2.</b>	<b>Application of Biocides . . . . .</b>	568
<b>2.1.</b>	<b>Factors Affecting Biocide Selection . . . . .</b>	568
<b>2.2.</b>	<b>Challenge Testing . . . . .</b>	569
<b>2.3.</b>	<b>Spoilage . . . . .</b>	570
<b>2.4.</b>	<b>Monitoring . . . . .</b>	570
<b>2.5.</b>	<b>Predetermined and Automatic Biocide Additions . . . . .</b>	572
<b>3.</b>	<b>References . . . . .</b>	572

The term microbiocide (or more simply biocide) is used to describe all agents that kill microbial life and thus includes antibiotics (→ Antibiotics), antimicrobial agents used in medicine (→ Chemotherapeutics), disinfectants (→ Disinfectants), and agricultural fungicides (→ Fungicides, Agricultural). This article will, however, deal mainly with the compounds used to prevent microbial growth in industrial products, particularly in the food industry, in cosmetics, pharmaceuticals and toiletries, in paints and plastics, in water cooling systems, and in paper manufacture. The use of microbiocides in wood preservation is discussed elsewhere (→ Wood Preservation).

**History.** Chemicals have been used since the very earliest times in the prevention of disease and the preservation of food. Notable examples were the use of burning sulfur to control the spread of plague and the widespread use of spicing, salting, and smoking to prevent the deterioration of food. The use of chemicals in earlier times was quite empirical since nothing was known about the mechanisms by which they effected the preservation of food or the control of disease. However, these empirical observations were supplemented by a more rigorous scientific investiga-

tion following the discovery of the microscope by VAN LEEUWENOEK in the 18th century.

VAN LEEUWENOEK demonstrated the presence of major classes of bacteria, protozoa, algae, and yeasts. The causal relationship between microorganisms and disease was established by the research work of BASSI and PASTEUR on the infection of silk worms by fungi and protozoa, respectively. Major contributions were subsequently made by KOCH and LISTER in the isolation and identification of pure bacterial strains as pathogens responsible for disease. Recognition of the fact that bacteria are responsible for disease and food spoilage created much interest in the development of chemicals for the control of these bacteria. Methods developed by KOCH and others were used in evaluating the effectiveness of these chemicals in destroying bacteria and curing disease. In the latter half of the 19th century, LISTER demonstrated that the use of phenol markedly reduced the incidence of serious infection during surgery. LISTER's work demonstrated the potential of chemical disinfectants in hospitals; subsequently, the use of less toxic and more efficient chemicals was extended to other areas of hospital practice.

The preventative role of chemical biocides was also becoming recognized in the industrial field. The use of biocides in metal working fluids, for example, is an important factor in maintaining product quality and the health of the work force. In oil recovery, biocides are used to control sulfate-reducing bacteria and to improve yields. In water cooling systems and paper production, added biocides prevent the formation of bacterial or fungal slimes thus avoid-

1,3-Dichloro-5,5-dimethylhydantoin [118-52-5] is sparingly soluble in water with which it reacts to give controlled release of hypochlorous acid. 1-Bromo-3-chloro-5,5-dimethylhydantoin [126-06-7] reacts with water to form both hypochlorous and hypobromous acids. The latter has a wider pH range of bactericidal activity than hypochlorous acid. When hypobromous acid comes into contact with nitrogenous waste, bromamines are formed which, unlike the chlorine analogues, retain a significant biocidal activity.

### 1.3. Iodine and Iodophores

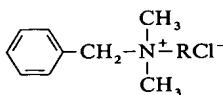
Iodine [7553-56-2] has a wide range of antimicrobial activity and is effective against gram-positive and gram-negative bacteria, mycobacteria, fungi, and viruses. It also kills bacterial spores after an extended contact time. The active species (the iodine molecule) is only sparingly soluble in water; iodine is therefore used as a solution of iodine in alcoholic potassium iodide.

Iodine stains the skin and may lead to sensitization of the skin and mucous membranes. Iodophores (iodine carriers) were developed in the 1950s in order to overcome these disadvantages. Iodophores are essentially complexes of iodine with various organic compounds which release iodine on demand. The most important complexes used are those with poly(propylene oxide) or poly(ethylene oxide), cationic surfactants (quaternary ammonium salts), or polyvinylpyrrolidone. The iodophores are used in hospitals primarily for skin disinfection, and also in dairy farming where they are important as udder washes in the prevention of bovine mastitis as, for example, the Iosan range of iodophores (Ciba-Geigy, Switzerland) or Iodel FD (Diversey, UK).

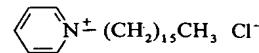
### 1.4. Quaternary Ammonium Compounds

Quaternary ammonium compounds are most effective against gram-positive bacteria at concentrations as low as 1:200 000. They are less active against gram-negative organisms: concentrations as high as 1:20 000 are required to control *Pseudomonas aeruginosa*. Further limitations of quaternary ammonium compounds are their inactivity at and below pH 3.5 and their reduced effectiveness under dirty conditions.

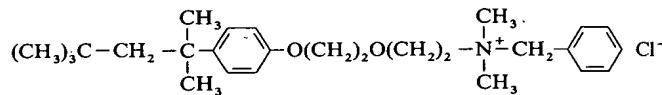
They are nontoxic and are used quite widely in hospitals, in the food industry, and as household disinfectants. Commercially important quaternary ammonium disinfectants are benzalkonium chloride [8001-54-5], benzethonium chloride [121-54-0], and cetylpyridinium chloride [123-03-5]:



Benzalkonium chloride

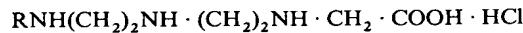


Cetylpyridinium chloride



Benzethonium chloride

Amphoteric quaternary ammonium disinfectants, usually alkylated aminocarboxylic acid derivatives, are also used commercially. The amphoteric have greater caustic stability than the normal quaternaries and are more easily removed from surfaces. This is a great advantage in the food industry where amphoteric are widely used. The formula of Tego 103 S (Goldschmidt, FRG) is given below:



### 1.5. Biguanides

Although the biguanides had been recognized as biologically active by IG Farben in the 1930s, their potential as active bactericides was first discovered by ICI in 1946 [1], [2] in the form of the biguanide polymer, poly(hexamethylene biguanide) hydrochloride [32289-58-0] (PHMB). Subsequently, 1,6-bis(4'-chlorophenylbiguanide) hexane [55-56-1] (chlorhexidine) was also found to be a potent biocide. Chlorhexidine and PHMB, are the major biguanide compounds which are used today as disinfectants and sanitizers [3].

*Chlorhexidine* is bactericidal at concentrations of 100 µg/mL and bacteriostatic at concentrations of 1 µg/mL. It is often formulated with 2-propanol and quaternary ammonium compounds. It is absorbed by the skin and is widely used as a topical disinfectant in hospitals. It is sold under the trade name of Hibitane (ICI, UK).


[Search](#) | [Contact us](#) | [Careers @ Lonza](#) | [Sitemap](#) |  Quick Search | Go

 Please read our Disclaimer  
 before proceeding. © 2005  
 Lonza Group Ltd, Switzerland

[Home](#) > [Products & Services](#) > [Products & Applications](#) > [Product Catalog](#) > [Products by Groups](#)

## Products by Groups

[send](#) [print](#)

Products & Services
<a href="#">Custom Manufacturing</a>
<b>→ Products &amp; Applications</b>
<a href="#">Product Catalog</a>
<a href="#">Products by Groups</a>
<a href="#">Products by Markets</a>
<a href="#">Websites: Products &amp; Services</a>
<a href="#">Sample &amp; Literature Request</a>
<a href="#">Personal Care &amp; Cosmetics</a>
<a href="#">Technology Platforms</a>

Company
<a href="#">About us</a>
<a href="#">Media Center</a>
<a href="#">Investor Relations</a>
<a href="#">Working at Lonza</a>
<a href="#">Worldwide</a>

**Product group**
 Quaternary Ammonium Compounds

**Description:**

Our quaternary ammonium compounds are used as disinfectants, sanitizers, deodorants, fungicides and cationic surfactants in formulations for household, institutional, industrial cleaners, water treatment, personal care and wood protection applications.

**Product subgroup**
 Dialkyl Quats

**Description:**

Dialkyl quats are a class of quaternary ammonium compounds generally used as disinfectants, sanitizers and algaecides. They are particularly effective against difficult to control organisms in hard water and in the presence of organic soil.

**Product**
 Bardap® 26

**Product Name**

Bardap® 26

**Chemical Name**

 N,N-Didecyl-N-methylpoly(oxyethyl)ammoniumpropionate  
 (in ca. 10%Ethylenglycol / ca. 18% Polyethylenglycol)

**Synonyms**

Didecylmethylpoly(oxethyl) Ammonium Propionate

**Form**

Liquid

**Quality**

Active ingredient (%): 70

**Description**

Bardap® 26 find uses in disinfectant for instruments and wood preservative due to its low corrosion properties.

**Attributes**

Globally sourced biocides are offered for applications and markets outside the US and Canada.

**Contact**
<mailto:contact.allendale@lonza.com>
**Product search**